

### **REMARKS**

Claims 40-64 are pending in this application. Applicant respectfully submits that he erred in numbering claims in the amendment and response filed on May 20, 2003, as two claims were inadvertently numbered "46." This error occurred without any intent to deceive, and Applicant apologizes for this error. Applicant has corrected the numbering of claims 46-64 by amendment herein. Applicant refers to both old (and new) claim numbering within this response when necessary. Claims 1-39 were cancelled previously. Claims 53-58 and 63 (new claim numbers 54-59 and 64) are withdrawn as being directed to a non-elected invention. Claims 40-47, 50 and 62 (new claim numbers 40-48, 51 and 63) stand rejected. Claims 48, 49, 51, 52, and 59-61 (new claim numbers 49, 50, 52, 53, and 60-62) are objected to. Claim 40 is amended herein. Support for this amendment can be found at page 4, lines 22-37, page 9, line 37 through page 10, line 6 and page 10, lines 14-23. No new matter is introduced by the above amendment to the claims. Claims 45, 46, 46, and 62 (new claim numbers 45-47 and 63) are cancelled herein without prejudice or disclaimer.

### **Objections**

Claims 48, 49, 51, 52, and 59-61 (new claim numbers 49, 50, 52, 53, and 60-62) are objected to as being dependent upon rejected base claims, but would be allowed if rewritten in independent form. Applicant herein amends claim 40 from which claims 48, 49, 51, 52, and 59-61 (new claim numbers 49, 50, 52, 53, and 60-62) depend either directly or indirectly. Thus, for the reasons presented below, Applicant believes claim 40 and dependent claims 48, 49, 51, 52, and 59-61 (new claim numbers 49, 50, 52, 53, and 60-62) are now in condition for allowance.

**Rejection Under 35 U.S.C. § 112, Second Paragraph**

Claim 46 (new claim number 47) stands rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Examiner alleges that the phrase "an analog of an amino acid" is not clear.

Applicant herein cancels former claim 46 (new claim 47), reciting the phrase "an analog of an amino acid," thus, rendering the rejection of this claim moot. Furthermore, the other claim 46 is cancelled herein as discussed below.

**Rejection Under 35 U.S.C. § 103(a)**

Claims 40-47, 50, and 62 (new claim numbers 40-48, 51 and 63) stand rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Adair, *et al.* (WO 91/09967, published 7/11/91) in view of Vijnh-Warrier, *et al.* (*Molecular Immunology* 32:1081-1092, 1995). In particular, the Examiner alleges that, "Adair, *et al.* teach methods of CDR grafting comprising acceptor framework and donor antigen binding regions of rodent antibodies (see abstract). Adair *et al.* also teach non-CDR residues which contribute to antigen binding and CDR contacting residues (see page 20-23)." Furthermore, the Examiner alleges that, "Vijnh-Warrier, *et al.* teach the nucleotide and amino acid sequence of the variable region of a *Pan troglodyte* antibody (see abstract). Vijnh-Warrier also teach several human germline variable region genes (see Figure 3, 4, and 5, and Table 1) and that chimpanzee mAbs are no more likely to elicit deleterious anti-immunoglobulin responses in humans than human mAbs (see page 1089)."

Applicant respectfully submits that for a proper obviousness rejection under 35 U.S.C. § 103, the Examiner has the burden of establishing *prima facie* with evidence or reasons that, *inter alia*, at the time of the invention, (1) the prior art of record would have suggested or

motivated one of ordinary skill in the art to carry out the combination and modification of the prior art as suggested by the Examiner to arrive at the claimed invention, and (2) "the prior art would also have revealed that in so making or carrying out, those of ordinary skill in the art would have a reasonable expectation of success. Both the suggestion [or motivation] and the reasonable expectation of success must be founded in the prior art, not in the appellants' disclosure." *In re Vaeck*, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991) (citations omitted).

Applicant herein amends claim 40 to recite:

An antibody comprising:

- a) a variable region comprising six complementarity determining regions (CDRs) from an antigen specific donor antibody of a rodent and acceptor framework comprising amino acid residues from an Old World Ape, wherein at least one CDR-contacting amino acid residue from the acceptor framework is replaced with a corresponding residue from the donor framework, and wherein said CDR-contacting residue contacts a CDR residue within said antibody by the group selected from coming within the van der Waals radius of said CDR residue, a salt bridge and a hydrophobic interaction; and
- b) at least one constant region from human.

Claims 45, 46, 46 and 62 (new claim numbers 45-47 and 63) are cancelled herein without prejudice or disclaimer, rendering the rejection of these claims moot.

Applicant respectfully submits that neither Adair, *et al.* nor Vijn-Warrier, *et al.* teach or suggest the instantly claimed antibodies. First, neither Adair, *et al.* nor Vijn-Warrier, *et al.* teach or suggest an antibody wherein an acceptor framework residue is substituted with a corresponding donor residue based on the acceptor framework residue contacting a CDR residue by coming within the van der Waals radius of the donor residue, or by a salt bridge or hydrophobic interaction. Second, the teachings of Adair, *et al.* and Vijn-Warrier, *et al.* are directed only to the variable region of an antibody. Neither suggests a chimeric variable

region comprising CDRs from rodent and framework from Old World Ape combined with at least one human constant region as Applicant instantly claims.

Adair, *et al.* disclose antibodies containing non-human CDRs grafted into a human framework. Adair, *et al.* focus on antigen binding of the variable region of such an antibody. To determine acceptor framework residues that may effect antigen binding, Adair, *et al.* subdivide these residues into the following groups: (1) surface residues near the CDR, (2) packing residues near the CDR, (3) residues at the variable domain interface between heavy and light chain; and (4) variable-constant region interface residues (see pages 20-23). Adair, *et al.* then provide Kabat numbers of acceptor residues that they considered important for donor residue substitutions. Applicant respectfully submits that Adair, *et al.* do not teach or suggest that CDR-contacting residues be characterized as "within the van der Waals radius of said CDR residue, a salt bridge and a hydrophobic interaction," as amended claim 40 recites.

Furthermore, Applicant submits that Adair, *et al.* do not teach or suggest a chimeric antibody comprising CDRs from rodent and framework regions from Old World Ape and also comprising at least one constant region from human. The teachings of Adair, *et al.* focus on CDR-grafting and residues effecting antigen binding, which are found in an antibody variable region. Adair, *et al.* do not discuss secondary immune functions such as complement fixation or Fc receptor binding involving an antibody's constant regions.

Vijh-Warrier, *et al.* merely disclose a comparison of variable regions of a single chimpanzee monoclonal antibody with variable regions of antibodies from similar human germplines. Vijh-Warrier, *et al.* demonstrate a homology between chimpanzee nucleic acid and amino acid sequences from the variable regions of C108G and "their closest human germline genes" (see page 1089). However, this comparison is only for selected variable regions from antibodies against HIV-1. Vijh-Warrier, *et al.* do not teach or suggest creating a

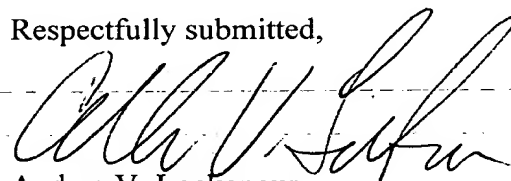
chimeric antibody with CDRs from rodent and framework regions from Old World Ape.

More importantly, Vijn-Warrier, *et al.* do not teach or suggest that an antibody comprising an Old World Ape framework also comprise at least one constant region from human.

Applicant respectfully submits that in view of the forgoing amendments and remarks, he has overcome the Examiner's rejection of claims 40-44, 47 and 50 (new claim numbers 40-44, 48 and 51) under 35 U.S.C. § 103. Reconsideration and withdrawal of these rejections is respectfully requested.

Applicant reserves the right to prosecute, in one or more patent applications, the claims to non-elected inventions, the cancelled claims, the claims as originally filed, and any other claims supported by the specification. Applicant thanks the Examiner for the Office Action and believe this response to be a full and complete response to such Office Action. Accordingly, favorable reconsideration and allowance of the pending claims is earnestly solicited. If it would expedite the prosecution of this application, the Examiner is invited to confer with the Applicant's undersigned attorney.

Respectfully submitted,



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